

10/014221

PHA 6157.2(3085/1)
PATENT

Cofe

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent of John S. Ng et al.

Patent No. 6,887,991

Issued May 3, 2005

Confirmation No. 2501

For PROCESSES FOR PREPARATION OF 9,11-EPOXY
STERIODS AND INTERMEDIATES USEFUL THEREIN

Certificate
JUN 06 2005
of Correction

May 25, 2005

**REQUEST FOR EXPEDITED ISSUANCE
OF CERTIFICATE OF CORRECTION UNDER 37 CFR 1.322**

TO THE COMMISSIONER FOR PATENTS,

SIR:

On studying the above-identified patent, the following errors, apparently made by the Patent and Trademark Office, were found (these errors are also noted on the attached form PTO-1050):

In column 253, claim 2, line 34, "steroid substrate comprises" should read -- steroid comprises --. (See Amendment B, claim 60, page 2, line 2).

In column 253, claim 2, line 37, "3-dialkoxy-5,7-lactone" should read -- 3-dialkoxy-5,7-lactone --. (See Amendment B, claim 60, page 2, line 5).

In column 254, claim 3, line 1, please add a space between "—" and "represents". (See Amendment B, claim 63, page 3, line 8).

In column 255, claim 4, line 1, please add a space between "—" and "represents". (See Amendment B, claim 64, page 4, line 11).

In column 256, claim 5, line 2, please add a space between "—" and "represents". (See Amendment B, claim 142, page 27, line 10).

In column 256, claim 5, line 3, "alpha- or beta-oriented" should read -- alpha- or beta-oriented --. (See Amendment B, claim 142, page 27, line 10).

In column 256, claim 6, line 34, "-CHR⁴ CHR⁵-" should read -- -CHR⁴-CHR⁵- --. (See Amendment B, claim 143, page 28, line 5).

In column 256, claim 6, line 40, please add a space between "—" and "represents". (See Amendment B, claim 143, page 28, line 10).

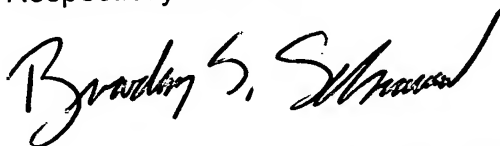
In column 256, claim 6, line 41, "alpha- or beta-oriented" should read -- alpha- or beta-oriented --. (See Amendment B, claim 143, page 28, line 10).

REMARKS

In accordance with 37 CFR 1.322, a copy of Amendment B dated July 20, 2004, is attached.

We respectfully request that a certificate of correction be issued.

Respectfully submitted,



Bradley S. Schammel, Reg. No. 54,667
SENNIGER POWERS
One Metropolitan Square, 16th Floor
St. Louis, Missouri 63102
(314) 231-5400

CERTIFICATE OF MAILING

I hereby certify that the foregoing Letter to the Patent and Trademark Office in the patent of John S. Ng et al., Patent No. 6,887,991, issued May 3, 2005 is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Post Issue, Certificate of Corrections Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on this 25th day of May, 2005.


Darlene Pearman

BSS/dep
*Enclosure

UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO. : 6,887,991 *Y3*

Page 1 of 1

DATED : May 3, 2005

INVENTOR(S): John S. Ng et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 253

Claim 2, line 34, "steroid substrate comprises" should read -- steroid comprises --.
Claim 2, line 37, "3-dialkoxy-5,7-lactone" should read -- 3-dialkoxy-5,7-lactone --.

Column 254

Claim 3, line 1, please add a space between "—" and "represents".

Column 255

Claim 4, line 1, please add a space between "—" and "represents".

Column 256

Claim 5, line 2, please add a space between "—" and "represents".
Claim 5, line 3, "alpha- or beta-oriented" should read -- alpha- or beta-oriented --.
Claim 6, line 34, "-CHR⁴ CHR⁵-" should read -- -CHR⁴-CHR⁵- --.
Claim 6, line 40, please add a space between "—" and "represents".
Claim 6, line 41, "alpha- or beta-oriented" should read -- alpha- or beta-oriented --.

MAILING ADDRESS OF SENDER:

PATENT NO. 6,887,991

Bradley S. Schammel
Senniger, Powers, Leavitt & Roedel
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St. Louis, Missouri 63102

No. of additional copies



This collection of information is required by 37 CFR 1.322, 1.323, and 1.324. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1.0 hour to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Attention Certificate of Corrections Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Express Mail No.
EV 416452565 US

PHA 6157.2 (3085/1)
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



Art Unit 1616

Application of John S. Ng, et al.

Serial No. 10/647,866

Filed August 25, 2003

Confirmation No. 2501

For PROCESSES AND PREPARATION OF 9,11-EPOXY
STEROIDS AND INTERMEDIATES USEFUL THEREIN

Examiner B. Badio

July 20, 2004

AMENDMENT B

TO THE ASSISTANT COMMISSIONER FOR PATENTS,

SIR:

This is in response to the Office action dated May 20, 2004.

Amendments to the Claims begin on page 2.

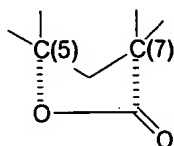
Remarks begin on page 41.

EV416452565US

IN THE CLAIMS:

Claims 1-58 (cancelled).

Claim 59 (presently amended): A process for the preparation of a 4,5-dihydro-5,7-lactone steroid compound, said lactone steroid being substituted with keto or dialkoxy at the 3-carbon, and comprising the moiety:



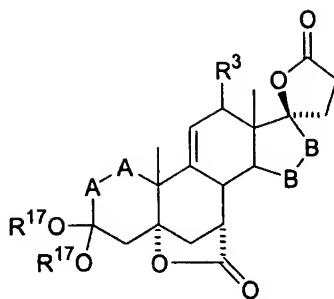
where C(5) represents the 5-carbon and C(7) represents the 7-carbon of the steroid structure of the lactone compound,
the process comprising:

converting a 7-cyano substituted steroid to the
corresponding 7-carboxylic acid substituted steroid, and
thereafter converting the 7-carboxylic acid substituted steroid
to the corresponding 5,7-lactone substituted steroid.

Claim 60 (presently amended): A process as set forth in claim 59 wherein the 7-carboxylic acid substituted steroid substrate comprises a 3-keto- Δ -4,5-7-carboxy steroid, and a ketal intermediate comprising a 3-dialkoxy-5,7-lactone is formed, said 3-dialkoxy-5,7-lactone being hydrolyzed under the acidic conditions to form the 3-keto-5,7-lactone.

Claims 61-62 (cancelled).

Claim 63 (previously amended): A process for the preparation of a compound corresponding to Formula E:



E

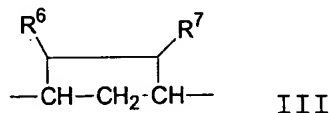
wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy;

R^{17} is C_1 to C_4 alkyl; and

-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:

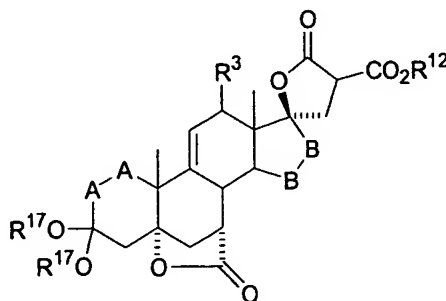


III

where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl and cyano and aryloxy;

the process comprising:

thermally decomposing a compound corresponding to Formula DE2 in the presence of an alkali metal halide, said compound of Formula DE2 having the structure:

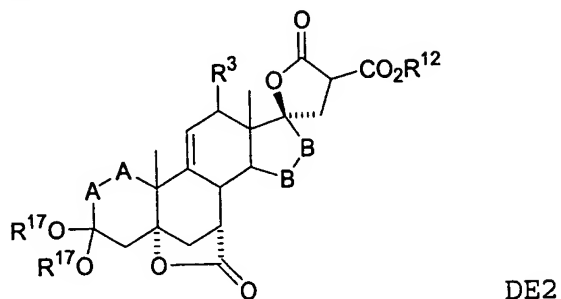


DE2

wherein R^{12} is C_1 to C_4 alkyl, and -A-A-, -B-B-, R^3 and R^{17}

are as defined above.

Claim 64 (previously amended): A process for the preparation of a compound corresponding to Formula DE2:



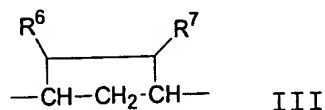
wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy;

R^{12} and R^{17} are independently selected from among C_1 to C_4 alkyl; and

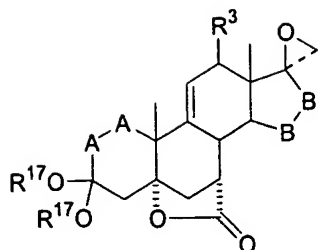
-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:



where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy;

the process comprising:

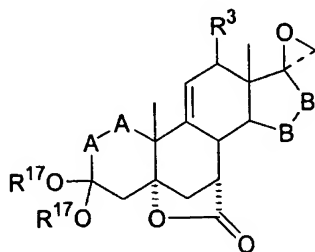
condensing a compound of Formula DE1 with a dialkyl malonate in the presence of a base, said compound of Formula DE1 having the structure:



DE1

wherein -A-A-, -B-B-, R^3 and R^{17} are as defined above.

Claim 65 (currently amended): A process for the preparation of a compound corresponding to Formula DE1:



DE1

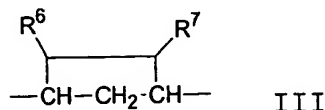
wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy;

R^{17} is C_1 to C_4 alkyl; and

-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:



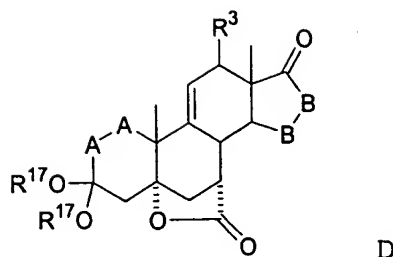
III

where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy;

the process comprising:

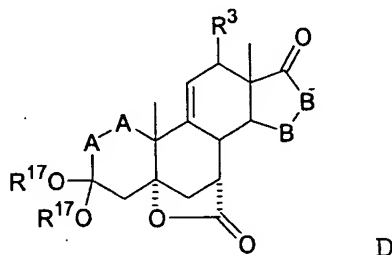
reacting a compound of Formula D with a sulfonium ylide in the presence of a base, said compound of Formula D having the

structure:



wherein -A-A-, -B-B-, R^3 and R^{17} are as defined above.

Claim 66 (previously amended): A process for the preparation of a compound corresponding to Formula D:



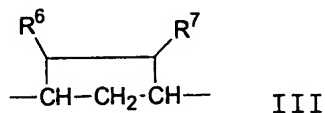
wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy;

R^{17} is C_1 to C_4 alkyl; and

-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:

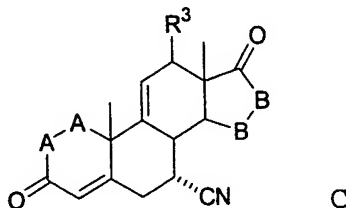


where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy;

the process comprising:

hydrolysis of a compound of Formula C to the 7α -carboxylic

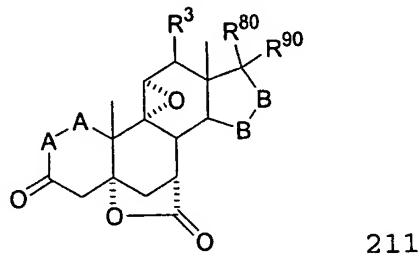
acid and reaction under acidic conditions with a trialkyl orthoformate, the compound of Formula C having the structure:



wherein -A-A-, -B-B- and R^3 are as defined above.

Claims 67-68 (cancelled).

Claim 69 (previously amended): A process for the preparation of a compound corresponding to Formula 211:

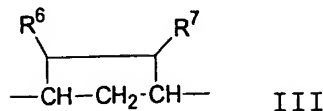


wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy; and

-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:



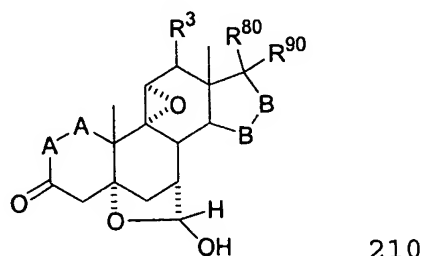
where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy;

R^{80} and R^{90} are independently selected from R^8 and R^9 , respectively or R^{80} and R^{90} together form keto;

R^8 and R^9 are independently selected from the group consisting of hydrogen, hydroxy, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, hydroxycarbonylalkyl, [alkoxycarbonyl] alkoxycarbonylalkyl, acyloxyalkyl, cyano and aryloxy, or R^8 and R^9 together comprise a carbocyclic or heterocyclic ring structure, or R^8 or R^9 together with R^6 or R^7 comprise a carbocyclic or heterocyclic ring structure fused to the pentacyclic D ring;

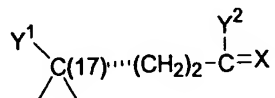
the process comprising:

oxidizing a compound of Formula 210, said compound of Formula 210 having the structure



where -A-A-, -B-B-, R^3 , R^{80} and R^{90} are as defined above.

Claim 70 (currently amended): A process as set forth in claim 69 wherein ~~R^8 and R^9~~ R^{80} and R^{90} together with C(17) comprise



where X represents two hydrogen atoms, oxo or =S;

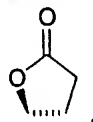
Y^1 and Y^2 together represent the oxygen bridge -O-, or

Y^1 represents hydroxy, and

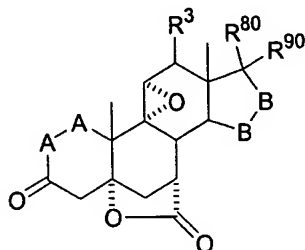
Y^2 represents hydroxy, lower alkoxy or, if X represents H_2 , also lower alkanoyloxy.

Claim 71 (currently amended): A process as set forth in claim 70

wherein ~~R⁸ and R⁹~~ R⁸⁰ and R⁹⁰ together with C(17) comprise



Claim 72 (currently amended): A process for the preparation of a compound corresponding to the Formula A211:



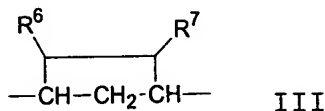
A211

wherein

-A-A- represents the group -CHR⁴-CHR⁵- or -CR⁴=CR⁵-;

R³, R⁴ and R⁵ are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy; and

-B-B- represents the group -CHR⁶-CHR⁷- or an alpha- or beta-oriented group:



III

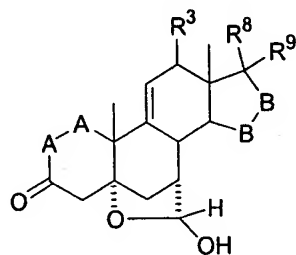
where R⁶ and R⁷ are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxy carbonyl, acyloxyalkyl, cyano and aryloxy; and

R⁸ and R⁹ are independently selected from the group consisting of hydrogen, hydroxy, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, [hydroxycarbonyl, alkyl] hydroxycarbonylalkyl, [alkoxycarbonyl] alkoxycarbonylalkyl, acyloxyalkyl, cyano and aryloxy, or R⁸ and R⁹ together comprise a

carbocyclic or heterocyclic ring structure, or R⁸ or R⁹ together with R⁶ or R⁷ comprise a carbocyclic or heterocyclic ring structure fused to the pentacyclic D ring;

the process comprising:

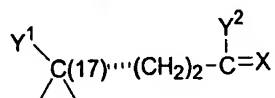
reacting a 3-keto-5,7-hemiacetal intermediate of Formula A209C with a peroxide oxidizing reagent, said compound of Formula A209C corresponding to the formula:



A209C

wherein -A-A-, -B-B-, R³, R⁸ and R⁹ are as defined above.

Claim 73 (currently amended): A process as set forth in claim 72 wherein ~~R⁸ and R⁹~~ R⁸⁰ and R⁹⁰ together with C(17) comprise



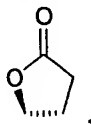
where X represents two hydrogen atoms, oxo or =S;

Y¹ and Y² together represent the oxygen bridge -O-, or

Y¹ represents hydroxy, and

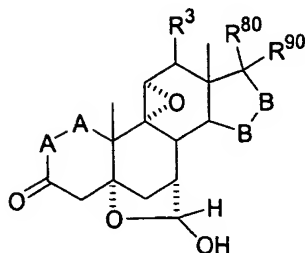
Y² represents hydroxy, lower alkoxy or, if X represents H₂, also lower alkanoyloxy.

Claim 74 (currently amended): A process as set forth in claim 73 wherein ~~R⁸ and R⁹~~ R⁸⁰ and R⁹⁰ together with C(17) comprise



Claim 75 (currently amended): A process for the preparation of a

compound corresponding to the Formula **A210**:



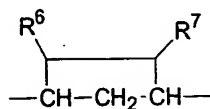
A210

wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy; and

-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:



III

where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy;

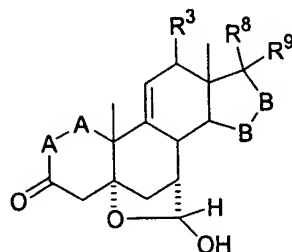
R^{80} and R^{90} are independently selected from R^8 and R^9 , respectively, or R^{80} and R^{90} together form keto;

R^8 and R^9 are independently selected from the group consisting of hydrogen, hydroxy, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy, or R^8 and R^9 together comprise a carbocyclic or heterocyclic ring structure, or R^8 or R^9 together with R^6 or R^7 comprise a carbocyclic or heterocyclic ring structure fused to the pentacyclic D ring;

the process comprising:

reacting a 3-keto-5,7-hemiacetal intermediate of Formula

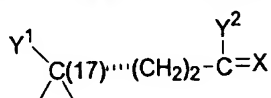
A209C with a peroxide oxidizing reagent, said compound of Formula A209C corresponding to the formula:



A209C

wherein -A-A-, -B-B-, R³, R⁸ and R⁹ are as defined above.

Claim 76 (currently amended): A process as set forth in claim 75 wherein ~~R⁸ and R⁹~~ R⁸⁰ and R⁹⁰ together with C(17) comprise



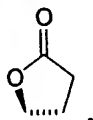
where X represents two hydrogen atoms, oxo or =S;

Y¹ and Y² together represent the oxygen bridge -O-, or

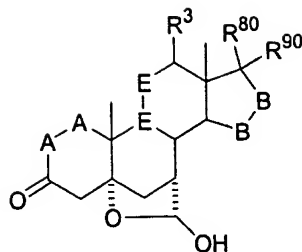
Y¹ represents hydroxy, and

Y² represents hydroxy, lower alkoxy or, if X represents H₂, also lower alkanoyloxy.

Claim 77 (currently amended): A process as set forth in claim 76 wherein ~~R⁸ and R⁹~~ R⁸⁰ and R⁹⁰ together with C(17) comprise



Claim 78 (currently amended): A process for the preparation of a compound corresponding to the Formula A209:



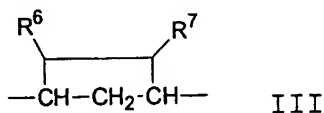
A209

wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy;

-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:



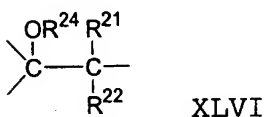
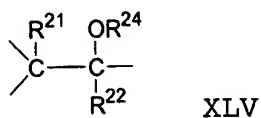
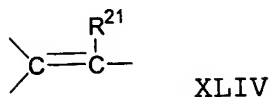
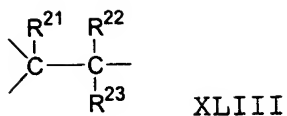
III

where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy;

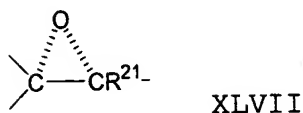
R^{80} and R^{90} are independently selected from R^8 and R^9 , respectively, or R^{80} and R^{90} together form keto;

R^8 and R^9 are independently selected from the group consisting of hydrogen, hydroxy, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, hydroxycarbonylalkyl, [alkoxycarbonyl], alkoxycarbonylalkyl, acyloxyalkyl, cyano and aryloxy, or R^8 and R^9 together comprise a carbocyclic or heterocyclic ring structure, or R^8 or R^9 together with R^6 or R^7 comprise a carbocyclic or heterocyclic ring structure fused to the pentacyclic D ring;

and -E-E- is selected from among:



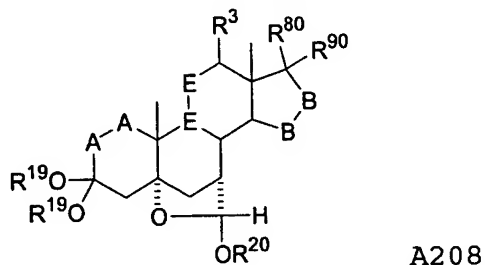
and



where R^{21} , R^{22} and R^{23} are independently selected from among hydrogen, alkyl, halo, nitro, and cyano; and R^{24} is selected from among hydrogen and lower alkyl;

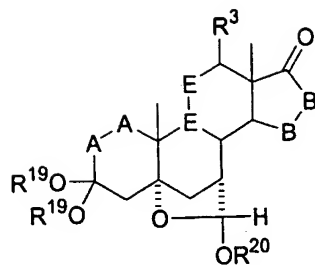
the process comprising:

hydrolyzing a compound corresponding to the Formula A208



wherein -A-A-, -B-B-, -E-E-, R^3 , R^{80} and R^{90} are as defined above; R^{19} is C_1 to C_4 alkyl or the $[\text{R}^{18}\text{O}]$ R^{19}O - groups together form an O,O-oxyalkylene bridge; and R^{20} is C_1 - C_4 alkyl.

Claim 79 (currently amended): A process for the preparation of a compound corresponding to Formula A205:



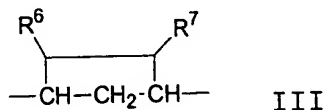
A205

wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy;

-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:

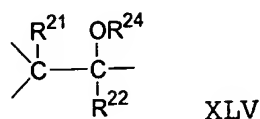
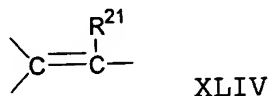
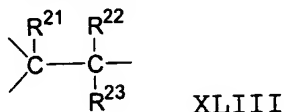


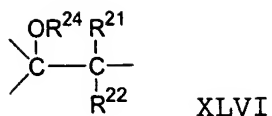
where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy;

R^{19} is C_1 to C_4 alkyl or the $[\text{R}^{18}\text{O}-]$ $\text{R}^{19}\text{O}-$ groups together form an O,O-oxyalkylene bridge; and

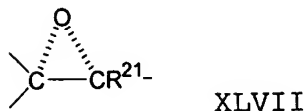
R^{20} is C_1 - C_4 alkyl; and

wherein -E-E- is selected from among:





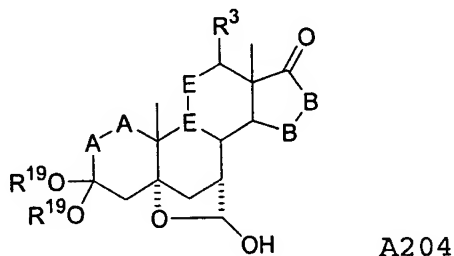
and



where R^{21} , R^{22} and R^{23} are independently selected from among hydrogen, alkyl, halo, nitro, and cyano; R^{24} is selected from among hydrogen and lower alkyl;

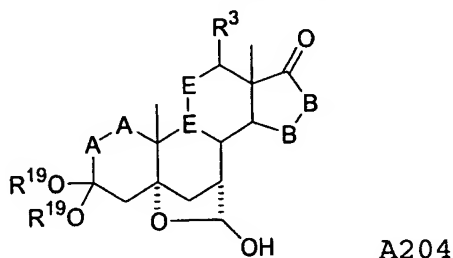
the process comprising:

reacting a compound corresponding to Formula A204 with a lower alcohol and an acid, said compound of Formula A204 having the structure:



wherein -A-A-, -B-B-, -E-E-, R^3 , and R^{19} are as defined above.

Claim 80 (currently amended): A process for the preparation of a compound corresponding to Formula A204:



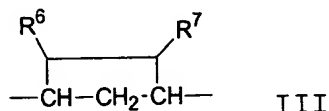
wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group

consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano aryloxy;

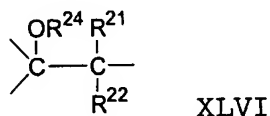
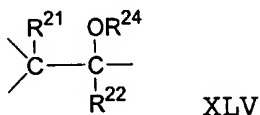
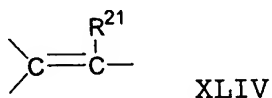
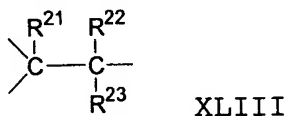
-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:



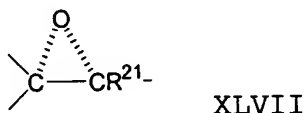
where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy; and

R^{19} is C_1 to C_4 alkyl or the $\text{R}^{19}\text{O}-$ groups together form an O,O-oxyalkylene bridge;

wherein -E-E- is selected from among:



and

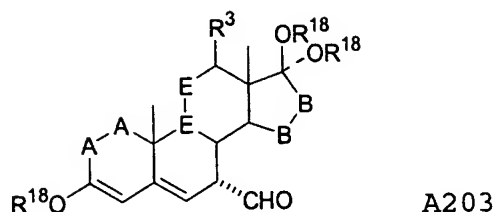


where R^{21} , R^{22} and R^{23} are independently selected from among hydrogen, alkyl, halo, nitro, and cyano; and R^{24} is selected from among hydrogen and lower alkyl;

the process comprising:

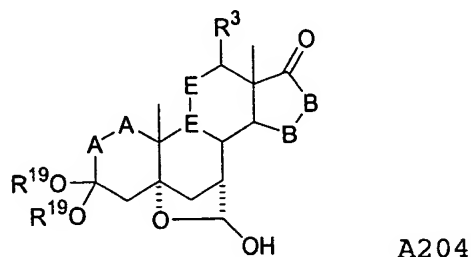
hydrolyzing compound corresponding to Formula A203, said

compound of Formula A203 having the structure:



wherein -A-A-, -B-B-, -E-E- and R^3 are as defined above, and R^{18} is C_1 to C_4 alkyl or the $R^{18}O$ - groups together form an O,O-oxyalkylene bridge.

Claim 81 (currently amended): A process for the preparation of a compound corresponding to Formula A204:

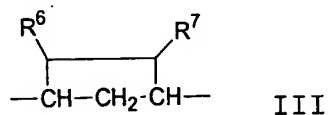


wherein

-A-A- represents the group $-CHR^4-CHR^5-$ or $-CR^4=CR^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy;

-B-B- represents the group $-CHR^6-CHR^7-$ or an alpha- or beta-oriented group:

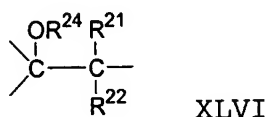
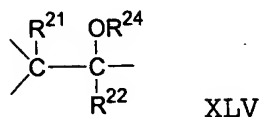
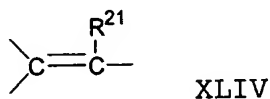
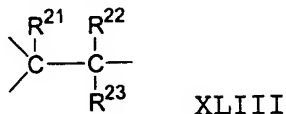


where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy; and

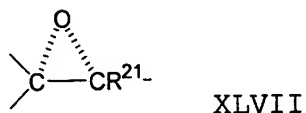
R^{19} is C_1 to C_4 alkyl or the $R^{19}O$ - groups together form an

O,O-oxyalkylene bridge; and

wherein -E-E- is selected from among:



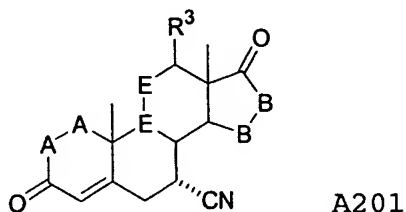
and



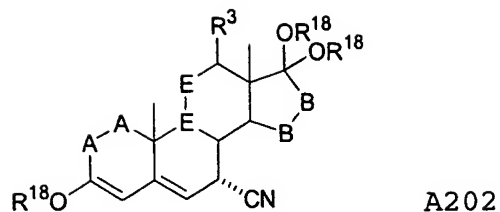
where R^{18} is C_1 to C_4 alkyl or the $\text{R}^{18}\text{O}-$ groups together form an O,O-oxyalkylene bridge; R^{21} , R^{22} and R^{23} are independently selected from among hydrogen, alkyl, halo, nitro, and cyano; and R^{24} is selected from among hydrogen and lower alkyl;

the process comprising:

protecting the keto substituents of a compound corresponding to Formula A201 by reaction with alkanol under acid condition in the presence of orthoformate, said compound of Formula A201 having the structure:



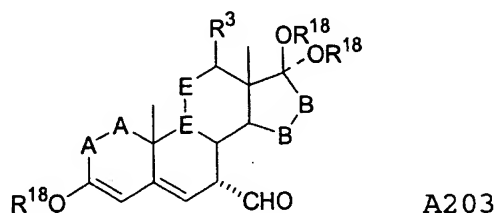
wherein -A-A-, -B-B-, -E-E- and R^3 , are as defined above, thereby producing a 3-enol ether intermediate corresponding to Formula A202:



wherein -A-A-, -B-B-, -E-E- and R^3 are as defined above, and R^{18} is C_1 to C_4 alkyl or the $R^{18}O$ - groups together form an O,O-oxyalkylene bridge; and

reducing said compound of Formula A202.

Claim 82 (currently amended): A process for the preparation of a compound corresponding to the formula A203:

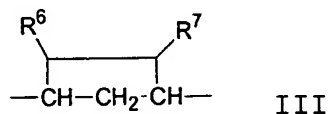


wherein

-A-A- represents the group $-CHR^4-CHR^5-$ or $-CR^4=CR^5-$;

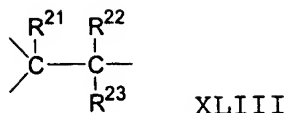
R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy;

-B-B- represents the group $-CHR^6-CHR^7-$ or an alpha- or beta-oriented group:

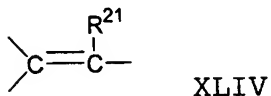


where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxy carbonyl, acyloxyalkyl, cyano and aryloxy; and

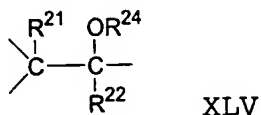
wherein -E-E- is selected from among:



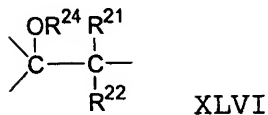
XLIII



XLIV

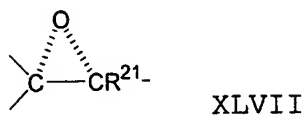


XLV



XLVI

and

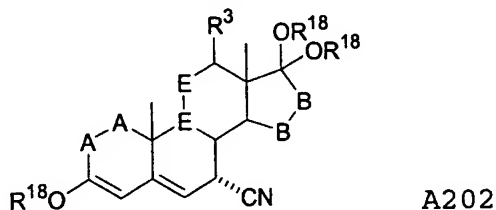


XLVII

where R^{18} is C_1 to C_4 alkyl or the $\text{R}^{18}\text{O}-$ groups at C-17 together form an O,O-oxyalkylene bridge; R^{21} , R^{22} and R^{23} are independently selected from among hydrogen, alkyl, halo, nitro, and cyano; and R^{24} is selected from among hydrogen and lower alkyl;

the process comprising:

reducing a compound corresponding to Formula A202:



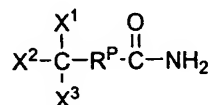
A202

wherein -A-A-, -B-B-, -E-E-, R^3 , and R^{18} are as defined above.

Claims 83-92 (cancelled).

Claim 93 (previously amended): A process for the formation of an epoxy compound comprising contacting a substrate compound having

an olefinic double bond with a peroxide compound in the presence of a peroxide activator, wherein said peroxide activator is chlorodifluoroacetamide or corresponds to a compound having to the formula



wherein

R^{P} is selected from the group consisting of alkenyl, alkynyl and $-(\text{CX}^4\text{X}^5)_2-$;

X^1 , X^2 , X^3 , X^4 and X^5 are independently selected from among halo, hydrogen, alkyl, haloalkyl and cyano and cyanoalkyl; and provided that at least one of X^4 and X^5 is halo.

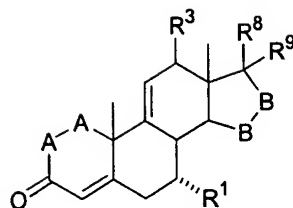
Claim 94 (previously amended): A process as set forth in claim 93 wherein and at least two of X^1 , X^2 and X^3 are halo or perhaloalkyl.

Claim 95 (previously amended): A process as set forth in claim 93 wherein all of X^1 , X^2 , X^3 , X^4 and X^5 are halo or perhaloalkyl.

Claims 96-97. (cancelled)

Claim 98 (previously amended): A process as set forth in claim 93 wherein said peroxide activator is selected from the group consisting of chlorodifluoroacetamide and heptafluorobutyramide.

Claim 99 (previously amended): A process as set forth in claim 93 wherein said substrate compound corresponds to the Formula:



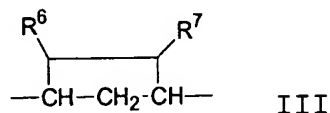
wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxy carbonyl, cyano and aryloxy;

R^1 represents an alpha-oriented lower alkoxy carbonyl or hydroxycarbonyl radical;

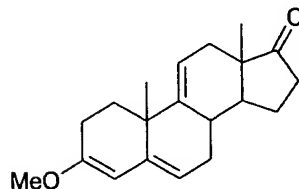
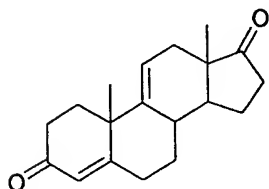
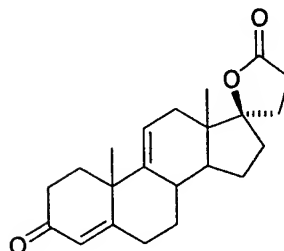
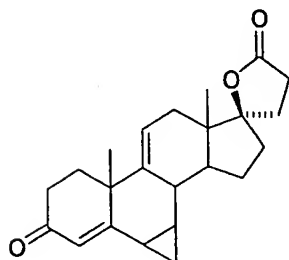
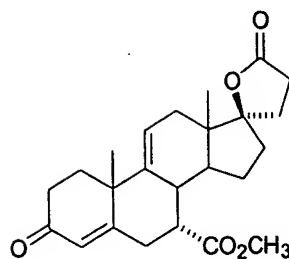
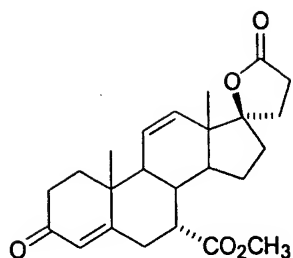
-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:



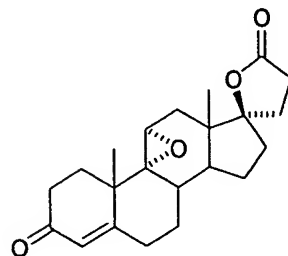
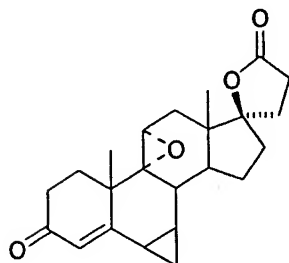
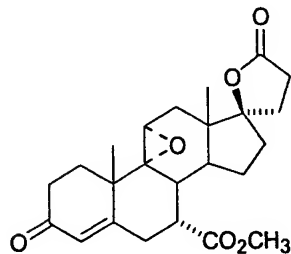
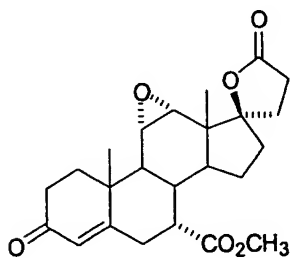
where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxy carbonyl, acyloxyalkyl, cyano and aryloxy; and

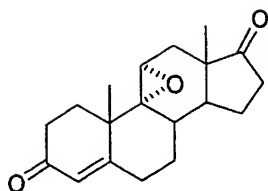
R^8 and R^9 are independently selected from the group consisting of hydrogen, hydroxy, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, hydroxycarbonylalkyl, [alkoxy carbonyl] alkoxy carbonylalkyl, acyloxyalkyl, cyano and aryloxy, or R^8 and R^9 together comprise a carbocyclic or heterocyclic ring structure, or R^8 or R^9 together with R^6 or R^7 comprise a carbocyclic or heterocyclic ring structure fused to the pentacyclic D ring.

Claim 100 (previously amended): A process as set forth in claim 93 wherein said substrate compound is selected from the group consisting of:

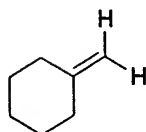
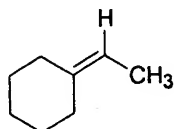
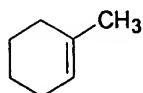
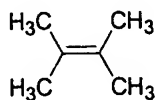
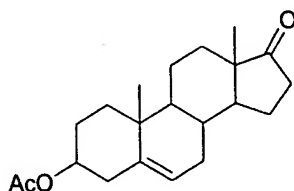


and a product of the epoxidation reaction is selected from the group consisting of:

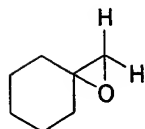
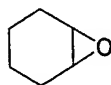
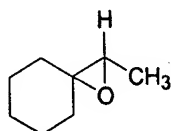
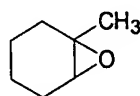
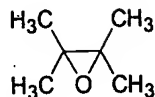
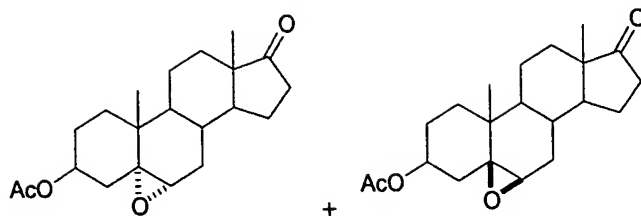




Claim 101 (previously amended): A process as set forth in claim 93 wherein said substrate compound is selected from the group consisting of:

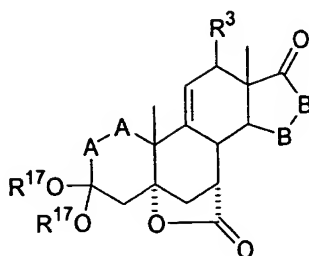


and a product of the epoxidation reaction is selected from the group consisting of:



Claim 102-140 (cancelled).

Claim 141 (previously amended): A compound corresponding to
Formula D:



D

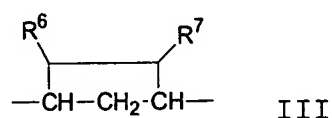
wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy;

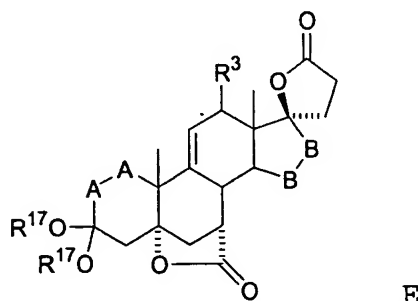
R^{17} is C_1 to C_4 alkyl; and

-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:



where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxyalkyl, acyloxyalkyl, cyano and aryloxy.

Claim 142 (previously amended): A compound corresponding to Formula E:



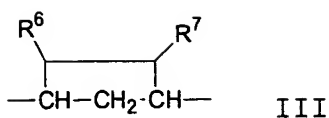
wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy;

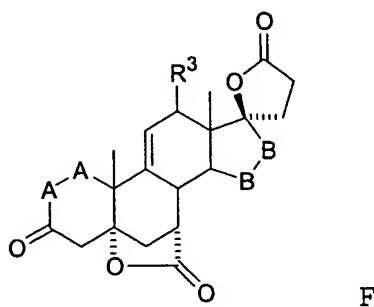
R^{17} is C_1 to C_4 alkyl; and

-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:



where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy.

Claim 143 (previously amended): A compound corresponding to Formula F:

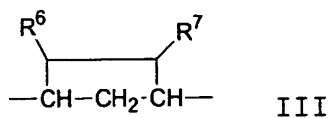


wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy; and

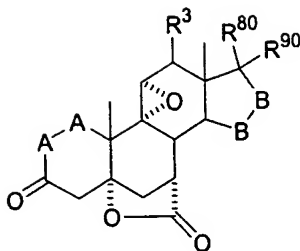
-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:



where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy.

Claim 144 (currently amended): A compound corresponding to

Formula A211:



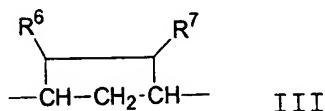
A211

wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy; and

-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:



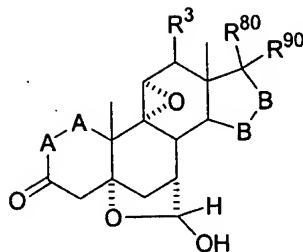
III

where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy;

R^{80} and R^{90} are independently selected from R^8 and R^9 , respectively or R^{80} and R^{90} together form keto; and

R^8 and R^9 are independently selected from the group consisting of hydrogen, hydroxy, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, hydroxycarbonylalkyl, [alkoxycarbonyl] alkoxycarbonylalkyl, acyloxyalkyl, cyano and aryloxy, or R^8 and R^9 together comprise a carbocyclic or heterocyclic ring structure, or R^8 or R^9 together with R^6 or R^7 comprise a carbocyclic or heterocyclic ring structure fused to the pentacyclic D ring.

Claim 145 (currently amended): A compound corresponding to
Formula A210:



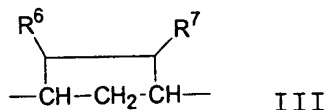
210

wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy; and

-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:



where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy;

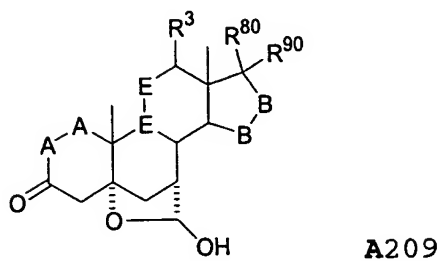
R^{80} and R^{90} are independently selected from R^8 and R^9 , respectively, or R^{80} and R^{90} together form keto; and

R^8 and R^9 are independently selected from the group consisting of hydrogen, hydroxy, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, [hydroxycarbonyl, alkyl]

hydroxycarbonylalkyl, [alkoxycarbonyl] alkoxycarbonylalkyl,

acyloxyalkyl, cyano and aryloxy, or R^8 and R^9 together comprise a carbocyclic or heterocyclic ring structure, or R^8 or R^9 together with R^6 or R^7 comprise a carbocyclic or heterocyclic ring structure fused to the pentacyclic D ring.

Claim 146 (currently amended): A compound corresponding to
Formula A209:

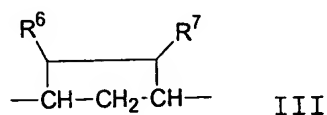


wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy; and

-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:

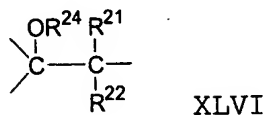
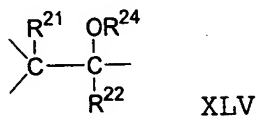
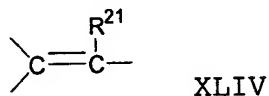
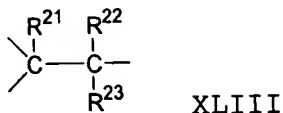


where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy;

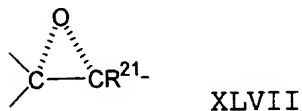
R^{80} and R^{90} are independently selected from R^8 and R^9 , respectively, or R^{80} and R^{90} together form keto;

R^8 and R^9 are independently selected from the group consisting of hydrogen, hydroxy, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, [hydroxycarbonyl, alkyl], hydroxycarbonylalkyl, [alkoxycarbonyl] alkoxycarbonylalkyl, acyloxyalkyl, cyano and aryloxy, or R^8 and R^9 together comprise a carbocyclic or heterocyclic ring structure, or R^8 or R^9 together with R^6 or R^7 comprise a carbocyclic or heterocyclic ring

structure fused to the pentacyclic D ring; and
-E-E- is selected from among:

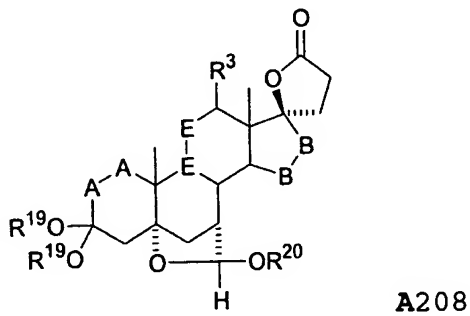


and



where R^{21} , R^{22} and R^{23} are independently selected from among hydrogen, alkyl, halo, nitro, and cyano; and
 R^{24} is selected from among hydrogen and lower alkyl.

Claim 147 (currently amended): A compound corresponding to
Formula A208:



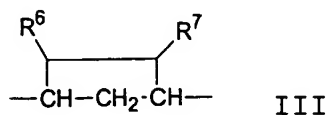
wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy,

hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy;

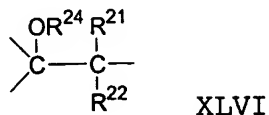
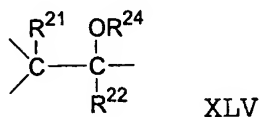
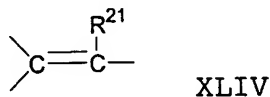
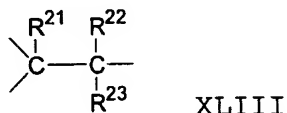
-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:



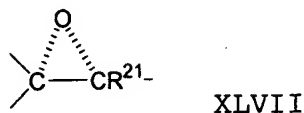
where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy; and

R^{20} is C_1 - C_4 alkyl; and

-E-E- is selected from among:



and



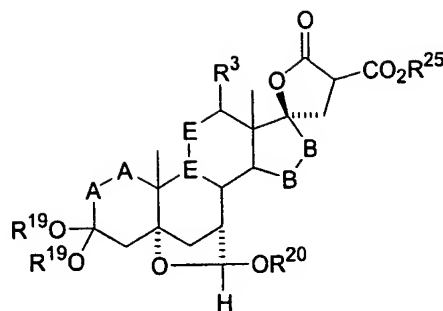
where R^{19} is C_1 to C_4 alkyl or the $\text{R}^{18}\text{O}-$ groups together form an O,O-oxyalkylene bridge;

R^{21} , R^{22} and R^{23} are independently selected from among hydrogen, alkyl, halo, nitro, and cyano; and

R^{24} is selected from among hydrogen and lower alkyl.

Claim 148 (currently amended): A compound corresponding to

Formula A207:



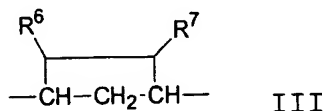
A207

wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy;

-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:

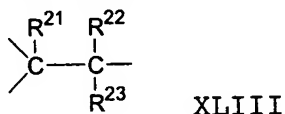


III

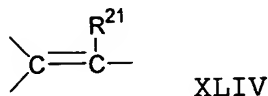
where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy; and

R^{20} is $\text{C}_1\text{-C}_4$ alkyl; and

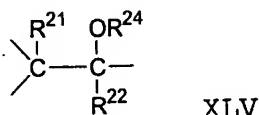
-E-E- is selected from among:



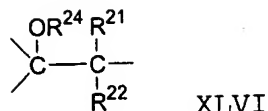
XLIII



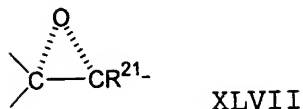
XLIV



XLV



and



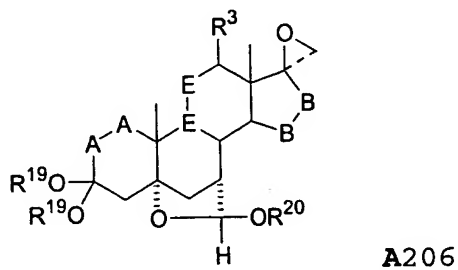
where R¹⁹ is C₁ to C₄ alkyl or the R¹⁸O- groups together form an O,O-oxyalkylene bridge;

R²¹, R²² and R²³ are independently selected from among hydrogen, alkyl, halo, nitro, and cyano;

R²⁴ is selected from among hydrogen and lower alkyl; and

R²⁵ is C₁ to C₄ alkyl.

Claim 149 (currently amended): A compound corresponding to Formula A206:

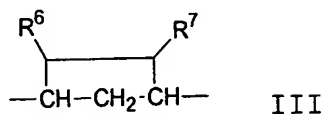


wherein

-A-A- represents the group -CHR⁴-CHR⁵- or -CR⁴=CR⁵-;

R³, R⁴ and R⁵ are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy;

-B-B- represents the group -CHR⁶-CHR⁷- or an alpha- or beta-oriented group:

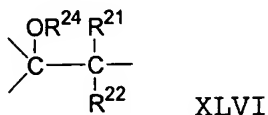
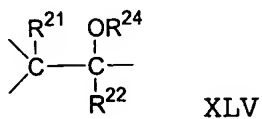
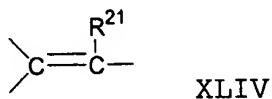
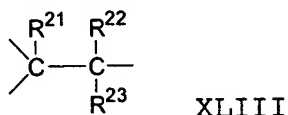


where R⁶ and R⁷ are independently selected from the group

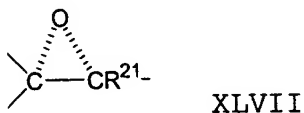
consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy;

R^{20} is C_1 - C_4 alkyl; and

-E-E- is selected from among:



and

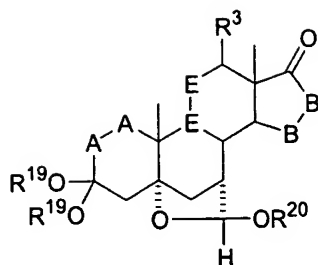


where R^{19} is C_1 to C_4 alkyl or the $R^{18}O$ - groups together form an O,O-oxyalkylene bridge;

R^{21} , R^{22} and R^{23} are independently selected from among hydrogen, alkyl, halo, nitro, and cyano;

R^{24} is selected from among hydrogen and lower alkyl.

Claim 150 (currently amended): A compound corresponding to Formula A205:



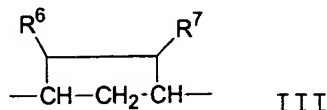
A205

wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy;

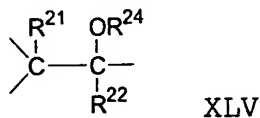
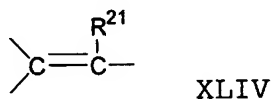
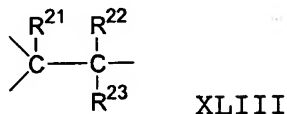
-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:

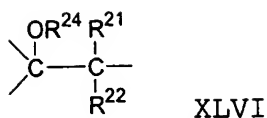


where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy; and

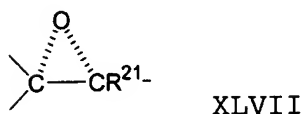
R^{19} and R^{20} is ~~are independently~~ selected from C_1 - C_4 alkyl; and

-E-E- is selected from among:





and

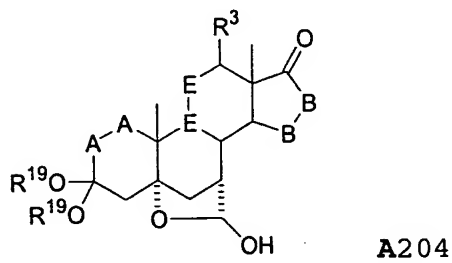


where R¹⁹ is C₁ to C₄ alkyl or the [R¹⁸O-] R¹⁹O- groups together form an O,O-oxyalkylene bridge;

R²¹, R²² and R²³ are independently selected from among hydrogen, alkyl, halo, nitro, and cyano;

R²⁴ is selected from among hydrogen and lower alkyl.

Claim 151 (currently amended): A compound corresponding to Formula A204:

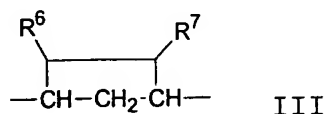


wherein

-A-A- represents the group -CHR⁴-CHR⁵- or -CR⁴=CR⁵-;

R³, R⁴ and R⁵ are independently selected from the group consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy;

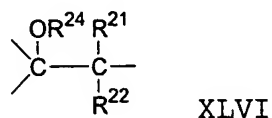
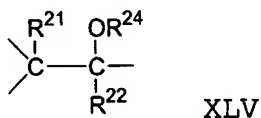
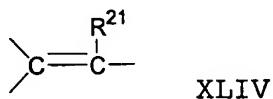
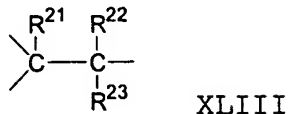
-B-B- represents the group -CHR⁶-CHR⁷- or an alpha- or beta-oriented group:



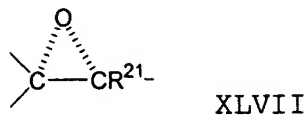
where R⁶ and R⁷ are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl,

acyloxyalkyl, cyano and aryloxy; and

-E-E- is selected from among:



and

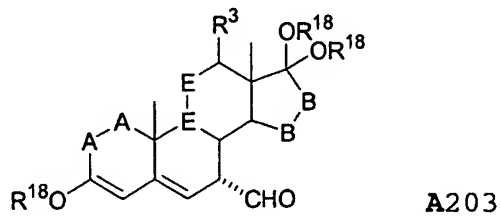


where $[\text{R}^{18}] \text{R}^{19}$ is C_1 to C_4 alkyl or the $[\text{R}^{18}\text{O}-] \text{R}^{19}\text{O}-$ groups together form an O,O-oxyalkylene bridge;

R^{21} , R^{22} and R^{23} are independently selected from among hydrogen, alkyl, halo, nitro, and cyano;

R^{24} is selected from among hydrogen and lower alkyl.

Claim 152 (currently amended): A compound corresponding to Formula A203:



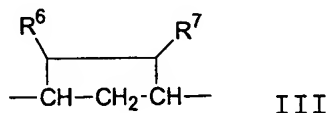
wherein

-A-A- represents the group $-\text{CHR}^4-\text{CHR}^5-$ or $-\text{CR}^4=\text{CR}^5-$;

R^3 , R^4 and R^5 are independently selected from the group

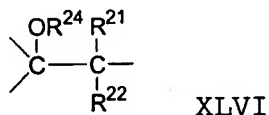
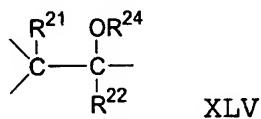
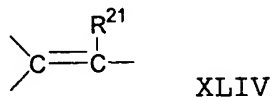
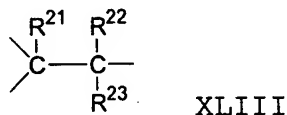
consisting of hydrogen, halo, hydroxy, lower alkyl, lower alkoxy, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, cyano and aryloxy;

-B-B- represents the group $-\text{CHR}^6-\text{CHR}^7-$ or an alpha- or beta-oriented group:

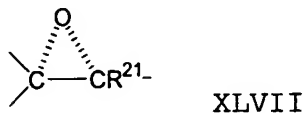


where R^6 and R^7 are independently selected from the group consisting of hydrogen, halo, lower alkoxy, acyl, hydroxyalkyl, alkoxyalkyl, hydroxycarbonyl, alkyl, alkoxycarbonyl, acyloxyalkyl, cyano and aryloxy; and

-E-E- is selected from among:



and



where R^{18} is C_1 to C_4 alkyl or the $\text{R}^{18}\text{O}-$ groups at C-17 together form an O,O-oxyalkylene bridge;

R^{21} , R^{22} and R^{23} are independently selected from among hydrogen, alkyl, halo, nitro, and cyano;

R^{24} is selected from among hydrogen and lower alkyl.

REMARKS

Reconsideration of the restriction requirement is respectfully requested.

The amendments to the claims are clarifying amendments and are supported in the original specification and the original claims.

Many of the claims that are separately grouped in accordance with the restriction requirement have at least one prominent feature in common; so that they could be properly combined for searching and examination without undue burden on the Office. In fact, many of the separately grouped claims have plural features in common. Moreover, many of the separately grouped claims are commonly classified, and all relate to two closely related process schemes that prominently include a 5,7-lactone intermediate.

It is respectfully submitted that the multiple splintering of closely related claims will be prejudicial to Applicants' assignee. The multiple divisional applications required to protect the claimed subject matter will impose excessive expense and consume scarce manpower resources in prosecuting closely related cases. For reasons also set forth below, it is respectfully submitted that dividing the application in accordance with the instant restriction requirement will not be in the public interest either.

All the claims are directed to processes and intermediates in the reaction steps described in schemes for the preparation of eplerenone or eplerenone derivatives of Formula I. More particularly, each claim is directed to a process for preparing intermediates or intermediates in process Schemes 9 and 10 as described in the specification, in which eplerenone or a derivative thereof is ultimately prepared. Many of these

intermediates share distinctive structural features.

It is respectfully submitted that splintering the claims of this application into 24 separate inventions is unreasonable, will result in wasteful duplication of effort, cause Applicants' assignee to incur untoward expense, and impose an unwarranted burden on Applicants' manpower resources. It would seem to effect a similar burden on the resources of the Office.

Applicants therefore respectfully request that the claims be regrouped so that all processes and compounds having a particular distinctive structural feature be examined in a single group, as outlined in the following table.

Common Feature	Class 540 (47+)	Class 540 (3+)	Class 549 (200+)	Class 549 (612+)
17-keto to 17- spiro lactone steroid		II, III, IV		
7-cyano to 5,7- lactone	I	V		
5,7-lactol to 5,7- lactone	VI			
epoxidation of 5,7- lactol or 5,7- lactone	VII, VIII			
hydrolysis of 5,7- acetal or protection of 5,7- lactol	IX, X			

conversion of 3-alkoxy- $\Delta^{3,4,5,6}$ steroid to 5,7-lactol	XI, XII			
5-cyano to 5 α -formyl	XIII			
epoxidation	XIV		XV	
3-ketal-5,7-lactone- $\Delta^{9,11}$ -17-keto steroid	XVI			
5,7-lactone- $\Delta^{9,11}$ -17-spirobutyrolactone steroid		XVII, XVIII		
3-keto-5,7-lactone and 5,7-lactol steroids	XIX			
3-keto-5,7-lactol-9,11-epoxy steroid	XX			
17-keto, 17-oxirane, 17-spirobutyrolactone steroid		XXI, XXII		
3-enol ether-7 α -formyl steroid				XXIV

Thus, referring to the table above, Applicants respectfully request that the claims be regrouped as follows:

1. Claim 63 (Group II), claim 64 (Group III) and claim 65 (Group IV) are directed to processes to prepare 3-ketal-

5,7-lactone- $\Delta^{9,11}$ steroids which have different structures at C(17). The 3-ketal and 5,7-lactone structures are distinctive and necessarily will be present in any prior art process that can reasonably form the basis for rejection of any claim of Groups II-IV. Not only do the Groups II-IV claims all require the 3-ketal-5,7-lactone- $\Delta^{9,11}$ feature, but all are in the same class and subclass, i.e., class 540 (3+).

2. Claims 50-60 (Group I) and claim 66 (Group V) are directed to the preparation of a 5,7-lactone steroid from a 7-cyano steroid. The presence of a 5,7-lactone structure is distinctive and these claims are in the same class, i.e., class 540.
3. Claims 69-71 (Group VI) is directed to the oxidation of a 5,7-lactol steroid to a 5,7-lactone steroid. They may reasonably remain separate from the other claim groups.
4. Claims 72-74 (Group VII) and 75-77 (Group VIII) are directed to epoxidation of a 3-keto-5,7-lactol- $\Delta^{9,11}$ steroid. The presence of a 3-keto-5,7-lactol- $\Delta^{9,11}$ structure is distinctive; moreover, these claims are in the same class and subclass, i.e., class 540 (47+).
5. Claim 78 (Group IX) and claim 79 (Group X) are directed to processes which comprise reverse reactions. Claim 78 is directed to a process for the hydrolysis of a 3-ketal-5,7-acetal to a 3-keto-5,7-lactol structure to form a 3-keto-5,7-lactol structure, whereas claim 79 is directed to the protection of a 3-keto-5,7-lactol structure to form a 3-ketal-5,7-acetal structure. Moreover, claims 78 and 79 are in the same class and subclass, i.e., class 540 (47+).
6. Claim 80 (Group XI) and claim 81 (Group XII) are directed to preparation of a 3-ketal-5,7-lactol-17-keto

steroid from a 3-alkoxy- $\Delta^{3,4,5,6}$ substrate. In claim 80, the starting material is a 7 α -formyl steroid. In claim 81, the starting material is a 3-keto-7 α -cyano steroid, which is converted to the 3-alkoxy- $\Delta^{3,4,5,6}$ intermediate that is in turn converted to a 5,7-lactol. Moreover, claims 80 and 81 are in the same class and subclass, i.e., class 540 (47+).

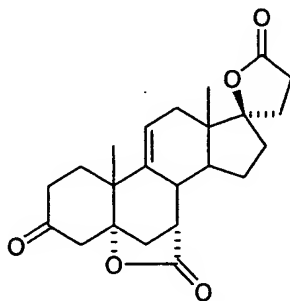
7. Claim 82 (Group XIII) is directed to reduction of a 3-alkoxy- $\Delta^{3,4,5,6}$ -7 α -cyano-17-ketal steroid substrate to form a 3-alkoxy- $\Delta^{3,4,5,6}$ -7 α -formyl-17-ketal steroid. It may reasonably be separated from the other claim groups.
8. Claims 93-101 (Groups XIV and XV) are directed to epoxidation where the dependent claims specifying steroid substrates are species to the generic claim 93. While claims specifying steroid substrates are patentably distinct from claim 93 specifying a substrate having an olefinic double bond, the epoxidation of the double bond in the substrate is the main feature of the claim.
9. Claim 141 (Group XVI) is directed to a 3-ketal-5,7-lactone- $\Delta^{9,11}$ -17-keto intermediate. It may reasonably be separated from the other claim groups.
10. Claim 142 (Group XVII) and claim 143 (Group XVIII) are directed to the 5,7-lactone- $\Delta^{9,11}$ -17-spirobutyrolactone intermediate E and Group XVIII is directed to the 5,7-lactone- $\Delta^{9,11}$ -17-spirobutyrolactone intermediate F. Moreover, claims 142 and 143 are in the same class and subclass, i.e., class 540 (3+).
11. Claims 144-145 (Group XIX) are directed to the 3-keto-5,7-lactone-9,11-epoxy and 3-keto-5,7-lactol-9,11-epoxy intermediates 211 and 210. They may reasonably be separated from the other claim groups.

12. Claim 146 (Group XX) is directed to the 3-keto-5,7-lactol-9,11-epoxy intermediate 209. It may reasonably be separated from the other claim groups.
13. Claims 147-148 (Group XXI), claim 149 (Group XXII) and claims 150-151 (Group XXIII) are directed to the intermediates involved in the spirolactonization reaction using a ylide reagent. For example, claims 147-148 are directed to 3-ketal-5,7-acetal-17-spirobutyrolactone and corresponding 17-malonic ester and 17-keto intermediates 208 and 207. Claim 149 is directed to the corresponding 17-oxirane intermediate 206 and claims 150-151 are directed to the corresponding 17-keto intermediate 205 and its predecessor 3-ketal-5,7-lactol-17-keto intermediate 204. Moreover, these claims are in the same class, i.e., class 540.
14. Claim 152 (Group XXIV) is directed to the 3-enol ether-7 α -formyl intermediate 203. It may reasonably be separated from the other claim groups.

Election

Applicants provisionally elect the claims of Group XVIII (claim 143) for examination in this application.

For search purposes, Applicants elect the following species.

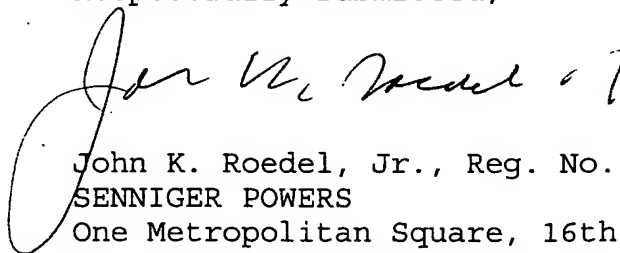


CONCLUSION

Favorable reconsideration and early allowance of all claims are respectfully requested. Applicants respectfully request a one-month extension of time to and including July 20, 2004, for filing a response to the May 20, 2004 Office action in this matter. Enclosed is a check in the amount of \$110.00 to cover the fee for the requested one-month extension of time.

The Commissioner is hereby authorized to charge to Deposit Account No. 19-1345 any fees under 37 CFR 1.16 and 1.17 which may be required during the entire pendency of this application

Respectfully submitted,



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May 25, 2005

Scott A. Williams, Esq.
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Post Office Box 1027
St. Louis, Missouri 63006

Re: U.S. Patent No. 6,887,991 entitled Processes for Preparation
of 9,11-Epoxy Steroids and Intermediates Useful Therein
Our File PHA 6157.2; Your Ref: 3085/1

Dear Scott:

* Enclosed for your records is a copy of a letter to the Patent and Trademark
Office, with a proposed Certificate of Correction, that we filed in connection with the
above-referenced patent.

Sincerely,

A handwritten signature in black ink, appearing to read "Bradley S. Schammel".

Bradley S. Schammel

BSS/dep
*Enclosure